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TITLE: Insulin-Like Growth Factor I Polymorphisms in Breast Cancer

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**13. Abstract** ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

Insulin-like growth factor I (IGF-I) is an important regulator of growth and differentiation, is known to inhibit apoptosis, is a potent mitogen for human breast cancer cells, and may influence proliferation of the cells of early breast cancer. A number of epidemiologic studies have evaluated the association between plasma IGF-I and breast cancer and have found that pre-menopausal women with higher levels of IGF-I show an elevated risk.

Genetic analysis has identified a highly polymorphic region of the IGF-I gene consisting of cytosine-adenine (CAn) dinucleotide repeats 1 kb upstream from the transcription start site. The relation between circulating IGF-I levels and the polymorphisms has been shown to vary according to the number of these CA repeats. This project is assessing the role of IGF-I polymorphisms in breast cancer, evaluating the relationship between the number of CA repeats in the IGF-I gene and plasma IGF-I levels, and determining if menopausal status confers differential risk of breast cancer in women with particular genotypes.

Progress on this project includes completion of laboratory training for techniques used in genotyping DNA samples. Aliquoting of samples has been completed and assay for PCR analysis has been developed and is currently being used to determine genotypes.

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**Insulin-like Growth Factor I Polymorphisms in Breast Cancer**

Annual summary report:

This project is investigating a highly polymorphic region of the IGF-I gene consisting of cytosine-adenine ($CA_n$) dinucleotide repeats 1 kb upstream from the transcription start site. A number of epidemiologic studies have evaluated the association between plasma IGF-I and breast cancer and have found that pre-menopausal women with higher levels of IGF-I show an elevated risk. Also, the relation between circulating IGF-I levels and this IGF-I polymorphism has been shown to vary according to the number of these CA repeats. For this project, the role of IGF-I polymorphisms in breast cancer will be assessed, the relationship between the number of CA repeats in the IGF-I gene and plasma IGF-I levels will be evaluated, and whether menopausal status confers differential risk of breast cancer in women with particular genotypes will be determined.

This project consists of three Tasks. Task 1 was stated to be untaken in months 1 – 24. Task 1 is still in progress and is on schedule. This task is to genotype genetic polymorphisms of the insulin-like growth factor I gene in 1,087 cases and 1,122 population-based controls on the Long Island Breast Cancer Study Project (Months 1 - 24). For this portion of the study, the majority of the time thus far has been spent in training and development of the polymerase chain reaction (PCR) assay. Intensive laboratory training was completed to learn basic laboratory techniques that would provide a base for the more technical skills that are required to perform PCR analysis. PCR techniques were learned over the course of several months and included the development of the assay that would be used in the genotyping of DNA samples for this project. An optimal assay for the region of interest has recently been developed to work using fluorescently labeled primers. Genotyping of the samples is currently underway and genotypes are being entered into a database.

Task 2 was stated to be completed in months 13 and 14. Task 2 is to conduct validation study of serum IGF-I levels using serum samples from 48 cases and 48 controls. Work on Task 2 will begin in the near future. Task 3 is to perform the final analysis and create final report and is to be carried out in months 24 – 36.

Key Accomplishments:

- Request for and arrival of shipment of 2,209 extracted DNA samples and 100 serum samples of cases and controls from the Long Island Breast Cancer Study Project (LIBCSP) main laboratory located at Columbia University in New York.
- Aliquots made of all 2,209 DNA samples.
- Creation of new laboratory database and assigning the samples new identification numbers in order to blind study personnel of the case-control status of DNA samples.
- Completed laboratory safety course.
- Completed intensive training in laboratory techniques including, but not limited to, PCR assay techniques used in this project to determine IGF-I genotypes, creating acrylamide gels, running PCR products on gels and determining size of fragments. Training for other laboratory techniques include troubleshooting problems that may occur with genotyping reactions and determining what can be done to make the reaction work.
- Developed PCR assay that best amplifies the region of interest for this project using fluorescently tagged primers.
- Genotyping completed on approximately 20 samples that were used during the assay development stage.

Reportable outcomes:

- Poster presentation at the Era of Hope meeting.